Application No. 10/007,574 Reply to Office Action of March 25, 2004

## **Amendments to the Specification:**

Please replace paragraph [0010] with amended paragraph [0010] as follows:

The invention relates to a method of generating a differentiated human cell of a [0010]selected type. The method comprises maintaining an isolated human KDR<sup>+</sup> stem cell in the presence of a differentiated mammalian (e.g., human) cell of the selected type. In this environment, the stem cell differentiates to become a differentiated human cell of the selected type. The stem cell can be maintained in the presence of the differentiated mammalian cell by maintaining it in contact with the mammalian cell or by maintaining it separated from the mammalian cell by a porous barrier, fi.e. a barrier that prevents intermixing of stem and mammalian cells, but permits fluid communication between the media in which the stem and mammalian cells are suspended. Alternatively, the stem cells can be maintained in a medium conditioned to reflect the presence of the differentiated mammalian cell therein (e.g., a medium in which the mammalian cell had previously been maintained or a synthetic medium formulated to replicate small molecules normally released by the mammalian cell in culture). The stem cell can be maintained in the presence of the differentiated cell in vivo (e.g., at the site of a damaged tissue) or in vitro (e.g., in a synthetic or other culture medium in a commercially available cell culture apparatus).

Please replace paragraph [0013] with amended paragraph [0013] as follows:

[0013] The invention includes a method of repairing a damaged human tissue. The method comprises maintaining an isolated human KDR<sup>+</sup> stem cell in the presence of a differentiated mammalian cell of a tissue (whether it is damaged or non-damaged) of the same type as the damaged tissue (or by maintaining the stem cell in a medium conditioned to reflect the presence therein of the differentiated cell). Following this treatment, the stem cell differentiates to become an altered cell that is differentiated from the initial stem cell. The altered cell can be a stem cell that has acquired the capacity to generate a tissue other than that of the tissue of its original residence (i.e., a tissue-exposed stem cell), even if the functionally different stem cell cannot be phenotypically distinguished until the stem cell further differentiates. The altered cell can also be a precursor or a terminally differentiated cell of the

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same type as the damaged tissue. The altered cell is provided to the damaged tissue, and the tissue is thereby repaired (i.e., either because altered cells of the damaged tissue type have been provided or because altered cells capable of differentiating to cells of the damaged tissue type have been provided). Damaged tissues that can be repaired in this manner include those associated with a disorders\_disorder\_such as stroke, ischemia, myocardial infarction, coronary artery disease, spinal cord injury, age-related tissue damage, Alzheimer's disease, Parkinson's disease, liver fibrosis, liver cirrhosis, chronic obstructive pulmonary disorder, compartment syndrome, multiple sclerosis, chronic inflammation, chronic infection, macular degeneration, and cataracts.

Please replace paragraph [0018] with amended paragraph [0018] as follows:

[0018] In one aspect, a KDR<sup>+</sup> cell comprises an isolated nucleic acid. The <u>nucleic acid</u> can be selected from the group consisting of a nucleic acid encoding adenosine deaminase, a nucleic acid encoding beta-globin, a nucleic acid encoding multiple drug resistance, an antisense nucleic acid complementary to a human immunodeficiency virus nucleic acid, an antisense nucleic acid complementary to a nucleic acid encoding a cell cycle gene, and an antisense nucleic acid complementary to a nucleic acid encoding an oncogene. The isolated nucleic acid can be operably linked to a promoter/regulatory sequence, such as one selected from the group consisting of a retroviral long terminal repeat and the cytomegalovirus immediate early promoter.